

Sex differences in outcome following sports-related concussion

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Object. Females comprise an increasing percentage of the athlete population across all age groups, and analysis of recent literature reveals that they sustain more concussions in collegiate sports. Results of human and animal studies indicate that females may have poorer outcomes after traumatic brain injury; however, no return-to-play guideline takes sex or other individual differences into account. In the present study the authors evaluated the influence of patient sex on objective neurocognitive performance and subjective reporting of symptoms following sports-related concussion.

Methods. According to preseason baseline neurocognitive computerized testing in 2340 male and female high school and collegiate athletes, individuals who sustained sports-related concussions (155 persons) were reevaluated using an alternate form of the cognitive test. Sex differences in the magnitude of cognitive change from baseline levels and the subjective experience of symptoms were analyzed. To account for the possible protective effects of helmets, comparisons were performed among females, males with helmets, and males without helmets; none of the female athletes wore helmets.

Female athletes had significantly greater declines in simple and complex reaction times relative to preseason baseline levels, and they reported more postconcussion symptoms compared with males. As a group, females were cognitively impaired approximately 1.7 times more frequently than males following concussions. Furthermore, females experienced more objective and subjective adverse effects from concussion even after adjusting for the use of helmets by some groups of male athletes (for example, in football).

Conclusions. Return-to-play decisions and concussion management must be objective and made on an individual basis, including consideration of factors such as patient sex rather than relying on a one-size-fits-all guideline.

KEY WORDS • sports-related concussion • mild head injury • sex-based difference • traumatic brain injury

As females increasingly participate in sports and other high-risk activities, a greater understanding of the role of patient sex in TBI outcome is needed.²⁰ In 1996, 2.4 million high school girls participated in school sports, representing 39% of the high school athlete population. This percentage represents an eightfold increase since 1971 when only 300,000 girls participated in high school sports.³⁷ More recent data indicate that females now comprise 42% of the athlete population at both the high school and college levels.⁴²

Started in 1945, the annual survey of catastrophic football injuries was expanded in 1982 through the establishment of the National Center for Catastrophic Sports Injury Research.³⁰ The expansion was partially motivated by the increasing participation of female athletes following Title

IX and by the lack of data on catastrophic injuries in female athletes. Analysis of data collected between 1982 and 1999 revealed that female athletes suffered fatalities or sustained permanent disabilities while participating in cheerleading, volleyball, softball, gymnastics, and field hockey and that more than 50% of these catastrophic injuries occurred due to cheerleading. In addition, these studies demonstrated that female athletes are at significant risk of sustaining sports concussions or more serious brain injuries. Data gathered by the National Collegiate Athletic Association Injury Surveillance System between 1997 and 2000 indicated that female college athletes experience a greater number of concussions during games than male college athletes, based on both raw numbers and per game exposure.¹¹ These researchers found that female collegiate athletes in soccer and basketball sustained significantly more concussions than their male counterparts. Although several studies have been focused on concussion following sports-related injury, none has been undertaken to analyze possible sex-based differences in symptom severity, constellation, or duration.

In the literature on mild head injury in which most trauma is typically due to motor vehicle accidents, there are few studies that do indicate a greater risk of poor outcome in fe-

Abbreviations used in this paper: AAN = American Academy of Neurology; ADHD = attention deficit hyperactivity disorder; ANOVA = analysis of variance; CI = confidence interval; CRI = Concussion Resolution Index; CRT = complex reaction time; LOC = loss of consciousness; MANCOVA = multivariate analysis of covariance; PS = processing speed; RCI = reliable change index; SE_{diff} = standard error of difference; SRT = simple reaction time; TBI = traumatic brain injury.

males. Females appear to have a greater likelihood of post-concussion syndrome at the 1-month follow up,⁴ a greater incidence of depression following mild TBI,²¹ and a greater number of persisting symptoms 1 year after mild brain injury.³⁵ Although most individuals typically make a full recovery from mild head injury, data from an epidemiological study at the University of Virginia in the early 1980s revealed that one third of the patients had persisting symptoms for at least 3 months.³² This result underscored the importance of studying the phenomenon of mild head injury and identifying characteristics that might relate to delayed recovery. Patient sex may be one of the variables that differentially affects recovery following mild head injury.

Among the literature on TBI are some notable studies during which investigators examined the role of patient sex on outcome. It is not surprising that these findings are inconsistent given that the demographic groups and the injury severity level differ across, and even within, studies.^{20,26} Despite the fact that males have approximately twice the risk of females for sustaining a TBI,⁹ data from a recent study in patients with moderate and severe TBI demonstrated that females had a mortality rate 1.28 times higher than that in males.²⁶ Additionally, the likelihood of a poor outcome in survivors was 1.57 times higher in females. A metaanalysis on sex-based differences in outcome following TBI revealed only nine studies in which the authors reported data according to sex.²⁰ Females demonstrated a poorer outcome in 17 of 20 variables (85%) with a mean effect size of -0.15 . Other researchers, however, have reported that females are more likely than males to return to school or work after moderate to severe brain injury.²³

The as yet limited research on the association between TBI and sex has yielded contrasting results. In the pediatric literature, authors of two studies found that girls outperformed boys on measures of learning and memory within 1 year after TBI.^{13,14} In contrast, authors of another study (data unpublished) found that girls experienced greater difficulties with executive function following significant brain injury.³⁸ Girls have also been reported to be more vulnerable to the long-term effects of cranial irradiation and chemotherapy.³⁹ Based on a review of the literature and their own prospective research, Kraus and colleagues²⁶ have asserted that future research in TBI should focus on the effects of sex as well as the pathophysiological basis of differential outcomes across the sexes.

Research in animals to investigate sex as a factor in TBI outcome has also yielded inconsistent results. Authors of one study found that estrogen treatment in rats before inflicting an experimental fluid-percussion brain injury provided protective effects in males and exacerbated the injury in females.¹⁶ Female rats have also been noted to have higher mortality rates following fluid-percussion injury. In hypotatremic conditions, depressed oxygen use and cerebral blood flow were observed in female rodents.²⁵ Data from these animal studies indicated a pathophysiological basis for the poorer outcome in the female sex following TBI. More recent research, however, has revealed that estrogen provided a neuroprotective effect, resulting in a better outcome in female mice compared with that in the male ones following experimental TBI inflicted using the murine impact-acceleration head injury method.²⁷ In addition, male mice had a 20% mortality rate, whereas no death occurred in the female mice.

A principal limitation of the human studies on concussion and TBI is the lack of preinjury data on patients, which especially limits the scope of research on sex-based differences in cognitive functions. For example, results of one recent study revealed significant sex differences between male and female college athletes, with females demonstrating faster and more accurate perceptual motor performance and better verbal fluency.³⁶ Sex differences in neuropsychological test performance in healthy athletes may in turn obscure sex differences in postconcussion cognitive functioning and recovery. Barth and colleagues² pioneered the principle of obtaining baseline preseason data on athletes prior to injury to increase the scope of scientific inquiry into mild head injury. This methodology, termed the "Sports-as-a-Laboratory model," is widely accepted as the gold standard for identifying and managing sports-related concussions and is now common in professional sports and college athletics.^{3,10,15} In previous studies¹⁷ we have demonstrated that the use of RCI scores, a means of appraising injured athletes individually posttrauma compared with their own unique baseline scores, is a superior method of determining and quantifying the severity of postconcussion cognitive symptoms. We therefore hypothesized that a greater understanding of potential sex differences in sports-related concussion would be possible by using a baseline model and RCI scores.

Clinical Material and Methods

Cognitive Performance Measures

The CRI, a web-based, brief computerized neurocognitive assessment tool, consists of six cognitive subtests that resolve to three summary speed factors: SRT, CRT, and PS. The CRI is sensitive to decreases in memory, reaction time, and speed of information processing immediately following concussion and until resolution of such typically transient neurocognitive dysfunction.¹⁷ All subtests were administered before trauma and again at each posttrauma evaluation. Statistical analyses of injured athletes' test performances are adjusted for test-retest reliability and for practice effects. Alternate forms are automatically provided.

When obtaining baseline measures, the subtests were preceded by a short questionnaire designed to gather demographic information, concussion history, and other pertinent medical information that might be useful in return-to-play decision making. Following head trauma, the cognitive subtests were preceded by questions about the athlete's symptom presentation immediately following injury (LOC, retrograde amnesia, dizziness, headache, and confusion/disorientation), which were answered by the athletic trainer or team physician who witnessed the injury, and the presence and intensity of postconcussion symptoms at testing time (headache, fatigue, memory problems, concentration difficulty, nausea, and so forth), which were rated by the athlete. All symptoms were surveyed at each postconcussion assessment. Although many symptoms are often recorded as absent, mild, moderate, or severe, for our purposes these symptom scales were truncated to the dichotomy of present or absent.

Participants and Procedures

Baseline CRI assessments were group administered in

TABLE 1

Summary of sports activities in 131 concussed athletes grouped according to sex

Group	No. of Patients (%)
females	
soccer	13 (35.1)
field hockey	7 (18.9)
lacrosse	5 (13.5)
basketball	4 (10.8)
cheerleading	3 (8.1)
other	5 (13.5)
males	
football	68 (72.3)
lacrosse	6 (6.4)
wrestling	6 (6.4)
other	14 (14.9)

computer labs via web-enabled desktop computers to athletes in contact sports at several US high schools and colleges as part of an ongoing research project. Institutional review board approval was obtained, as was informed consent from all adult athletes and from parents of athletes younger than 18 years of age. Following a concussion, athletes underwent follow-up tests according to the clinical judgment of the athletic trainer, team physician, or psychologist in charge of care, typically at 1- to 2-day intervals, until all symptoms resolved. For the current analysis, only data collected during the first follow up were used for comparisons with baseline performance levels. No other performances were included in the analyses.

Results

One hundred fifty-five athletes sustained concussions as determined at the time of the injury by an athletic trainer or physician using the Standardized Assessment of Concussion²⁹ and/or a symptom inventory. Of these athletes, 117 (75.5%) were male and 38 (24.5%) were female. Baseline cognitive performances on the CRI did not differ according to patient sex, ethnicity, age (high school compared with college), or history of learning disability or ADHD. Because analysis of postconcussion performances on the CRI according to patient sex was our interest, possible con-

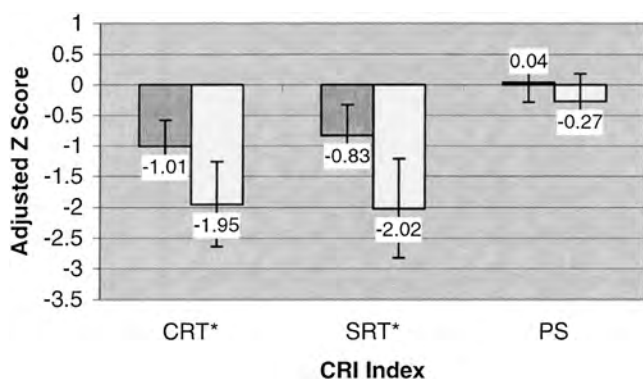


FIG. 1. Bar graph demonstrating mean RCI scores on CRIs together with 95% CIs on follow up. Shaded bars represent men; white bars represent women. * $p < 0.05$.

TABLE 2

Two indices of concussion severity grouped according to sex

Grading Criteria	No. of Patients (%)	
	Males	Females
Cantu grade		
I	45 (47.9)	15 (40.5)
II	22 (23.4)	10 (27.0)
III	27 (28.7)	12 (32.5)
AAN grade		
I	10 (10.6)	3 (8.1)
II	67 (71.3)	32 (81.9)
III	17 (18.1)	4 (10.8)

found were examined. Ethnic representation (Caucasian compared with non-Caucasian) differed significantly according to sex ($\chi^2 = 8.4$, $p = 0.004$), with Caucasians being overrepresented in the female group (86.8 compared with 61.5%). Note, however, that results of ANOVA revealed no difference between ethnic groups on the CRIs at the initial postconcussion assessment, indicating that potential differences based on sex would not be confounded by differences in the ethnic make-up of the two groups. A self-reported history of a learning disability or ADHD also differed significantly according to sex ($\chi^2 = 6.35$, $p = 0.012$), with such diagnoses being overrepresented in the male group (19.7 compared with 2.6%). Results of ANOVA revealed significant differences in postconcussion performances according to learning disability or ADHD, with those affected by such disabilities performing significantly slower on two of the three CRI speed indices (CRT: $F = 6.52$; $df = 1$, 153 [sample size minus two conditions in ANOVA]; $p = 0.012$ and PS: $F = 8.82$; $df = 1$, 153; $p = 0.003$). Because persons with a learning disability or ADHD were disproportionately male, this group of 24 athletes was excluded from further analyses to avoid confounding findings on sex and concussion.

Thus, of the 131 athletes studied further, 94 (71.8%) were males and 37 (28.2%) were females. There was an approximately equal number of high school and college athletes (47.3 compared with 52.7%, respectively), although women were overrepresented in the high school group (64.9 compared with 35.1%). Similarly, although the mean age for the entire group was 18.72 ± 2.1 years (standard deviation, range 14.3–23.8 years), males were significantly older than females (19.2 compared with 17.5 years; $F = 17.9$; $df = 1$, 129; $p < 0.001$). Because of the age discrepancy, analyses of age and age-based sex differences were performed for self-reported symptoms and CRI baseline, follow up, and baseline follow-up difference scores, with no significant age or age/sex interactions identified. Sixty-nine percent of the athletes identified themselves as Caucasian, 23% as African-American, and 8% as other. (Note that results of an ANOVA indicated that in the group excluded for learning disability and ADHD, there was no difference in baseline CRI scores based on sex, ethnicity, or age, thus revealing that the index is not ethnicity biased.) In 54% of the athletes, the incurred injury represented the first ever concussion, in 26% the second, in 11% the third, and in 9% the fourth or more; these frequencies did not differ significantly according to sex. Approximately 75% of the males sustained con-

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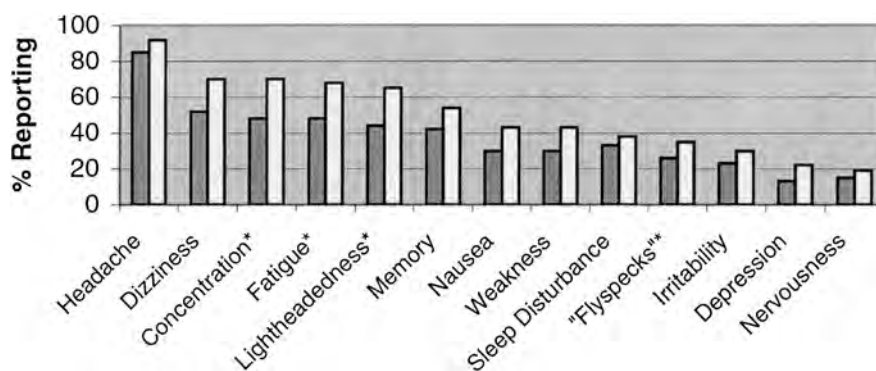


FIG. 2. Bar graph depicting self-reported symptoms on follow up according to patient sex. Shaded bars, males; white bars, females. * $p < 0.05$.

cussions while playing football and 33% of the females did so while playing soccer. Table 1 details the sports activities by sex. Males underwent their first postinjury assessment sooner than did females (mean 2.8 compared with 3.8 days, respectively; Mann-Whitney $\chi^2 = -2.3$, $p = 0.021$).

Severity of concussion was determined using two methods, the AAN³¹ and Cantu grading criteria,^{7,8} which were applied to each case based on contemporaneous reports by the athletic trainer or team physician who had witnessed the injury and was involved in the athlete's follow-up care. Table 2 depicts concussion severity graded according to both AAN and Cantu criteria stratified by sex. There was no difference between males and females in injury severity based on either of these criteria, although males did experience LOC approximately twice as frequently as females (18 compared with 11%, respectively). In keeping with our previous research, LOC did not correlate significantly with any outcome variable.

To assess differences in postconcussion CRI performance relative to baseline levels, RCI scores were calculated for the three speed factors in each athlete according to the following formula: $[(x_2 - x_1)/SE_{diff}] (-1)$.¹⁷ By multiplying the RCI z score by -1 , slower speeds following injury appeared as negative z scores, and faster postinjury performances as positive ones. To test whether there were differences in postconcussion objective and self-reported sequelae according to sex, a MANCOVA was performed using sex as the independent variable, RCI scores for each of the three CRI speed factors and total number of symptoms as dependent variables, and time to follow up as a covariate. The time to follow up correlated significantly with the extent of the cognitive performance decrease compared with baseline levels regardless of sex; in fact, longer time periods were associated with more minor decreases. Patient age, another variable that differentiated the two groups, did not correlate with the extent of the performance decrease compared with baseline, and so was not included as a covariate.

The overall model was significant for sex (Hotelling $T = 0.076$, $F = 2.36$, $p = 0.05$). Group comparisons were significant for CRT ($F = 5.13$, $p = 0.025$), SRT ($F = 6.20$, $p = 0.014$), and number of symptoms ($F = 5.41$, $p = 0.022$), but not for PS ($F = 1.41$, $p = 0.238$). Females consistently experienced greater declines in cognitive function and demonstrated more symptoms. Figure 1 depicts the mean RCI

z scores and 95% CIs for the two sex groups, adjusted for time to follow up, illustrating the greater performance declines on the CRI factors in females. In addition to the three CRI RCI scores, the number of symptoms reported by athletes at the time of the initial postconcussion evaluation was treated as a dependent variable reflective of the severity of postconcussion sequelae. The frequency of cognitive impairment based on sex is presented in Fig. 2. Although women reported concentration problems, fatigue, lightheadedness, and seeing fliespecks significantly more often than did men, the constellation of symptoms were remarkably similar between the sexes. Figure 3 depicts the mean number of symptoms together with 95% CIs reported by males compared with those reported by females.

To determine the clinical significance of these differences, athletes were classified as "cognitively impaired" if any one of their RCI scores indicated a decrease of more than $1.645 SE_{diff}$ ($p \leq 0.05$) from baseline levels at the postconcussion assessment. A z score of -1.645 was chosen as the threshold for determining a significant decline from baseline levels because a decrease of this size is associated with a probability value of 0.05. Approximately 57% of the females were cognitively impaired compared with 33% of the males, which represented a significantly greater frequency ($\chi^2 = 6.27$, $p = 0.012$).

We hypothesized that females might experience more



FIG. 3. Bar graph exhibiting the mean number of symptoms reported on follow up according to patient sex together with 95% CIs. Shaded bars, males; white bars, females; $p < 0.05$.

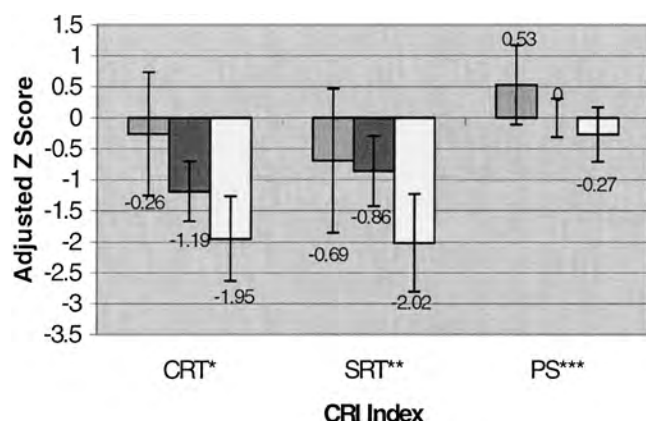


FIG. 4. Bar graph exhibiting mean RCI scores on CRIs together with 95% CIs on follow up. *Scores in females (white bars) were lower than those in males without helmets (light gray bars), $p < 0.01$; scores in females were lower than those in males with helmets (dark gray bars), $p < 0.15$. **Scores in females were lower than those in males without helmets, $p < 0.15$; scores in females were lower than those in males with helmets, $p < 0.05$. ***Speeds in females were lower than those in males without helmets, $p < 0.05$.

symptoms and demonstrate significant declines in cognitive function more frequently than males because few females wore headgear of any type, whereas most male athletes were football players, who were equipped with helmets. Therefore, we divided the male athlete group into those with and those without helmets and performed a MANCOVA using females (all of whom were unhelmeted), unhelmeted males, and helmeted males as the independent variable, the RCIs of the three CRI factors and the number of symptoms as dependent variables, and the time to follow up as a covariate. The overall model was significant for the patient sex helmet variable (Hotelling $T = 0.146$, $F = 2.25$, $p = 0.03$). Group comparisons were significant for CRT ($F = 4.00$, $p = 0.02$), SRT ($F = 3.11$, $p = 0.05$), and number of symptoms ($F = 3.74$, $p = 0.03$). Results of pairwise comparisons indicated that females demonstrated significantly slower response speed on the CRT and PS, a marginally slower SRT, and more symptoms compared with those in unhelmeted males. Females also had significantly slower response speed on the SRT and significantly more symptoms than those in helmeted males, whose performance generally occupied a middle ground between the two groups of unhelmeted athletes. Figure 4 depicts the mean RCI z scores and 95% CIs for the three groups, adjusted for time to follow up, illustrating the more severe declines experienced by females on the CRI factors. Figure 5 depicts the mean number of symptoms with 95% CIs reported by females, males without helmets, and males with helmets.

To determine the clinical significance of these differences, athletes were classified as cognitively impaired if any one of the RCI scores indicated a decrease of more than $1.645 \text{ SE}_{\text{diff}}$ ($p \leq 0.05$) from baseline levels at the post-concussion assessment. Table 3 shows that more than twice as many unhelmeted females (57%) were cognitively impaired compared with unhelmeted males (28%), and that helmeted males experienced impairment in 34% of the cases. The distribution of these frequencies was significant ($\chi^2 = 6.52$, $p = 0.038$). Of additional interest, the Mantel–

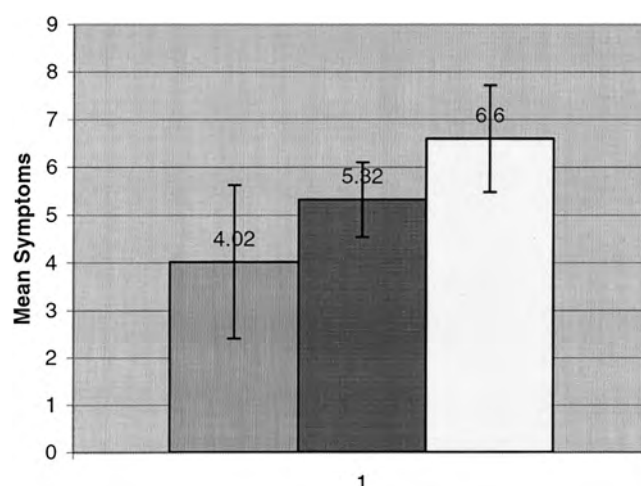


FIG. 5. Bar graph demonstrating the mean number of symptoms as well as CIs reported on follow up by males with helmets (dark gray bars), males without helmets (light gray bars), and females (white bars). Females had more symptoms than males without helmets, $p = 0.01$; females had more symptoms than males with helmets, $p = 0.05$.

Haenszel linear-by-linear association value of 5.68 ($p = 0.017$) indicated that, clinically, the same linear relationship as that observed in the ANOVAs was present.

Discussion

Since Title IX was passed in 1972, females have been participating in sports in increasing numbers. Surprisingly, the present study appears to be the first effort objectively to compare neurocognitive sequelae in male and female athletes following sports-related concussion. In this prospective study in high school and college athletes, we examined the relationship of patient sex to the severity of cognitive decline and the number of self-reported symptoms. First, we identified a significantly more severe decline in females on measures of SRTs and CRTs, relative to preseason baseline levels. Second, females self-reported significantly more symptoms following concussion compared with males. These sex differences were evident when comparing males and females in terms of both the degree of cognitive change from baseline levels and the frequencies of impaired cognitive performance. In the former case, the decreases in female cognitive performance levels were approximately $1 \text{ SE}_{\text{diff}}$ greater than those in males. In the latter case, females were cognitively impaired approximately 1.5 times more often than males following concussion (57 compared with 37%, respectively). These findings did not appear to be due to differences in injury severity, patient age or ethnicity, baseline performance levels, or time to follow up. In fact, females demonstrated significantly greater changes from baseline cognitive performance and significantly more symptoms following concussion despite being evaluated a mean of 24 hours later than males.

Patient age, which did differ between men and women in our sample, was not significantly correlated with CRI baseline, follow-up, or baseline follow-up difference scores or with the number of self-reported symptoms. Furthermore,

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there was no significant interaction between patient age and sex for these same scores and symptoms.

An additional hypothesis and a possible explanation for our findings was that helmets might provide protection for male athletes, the majority of whom were football players; however, women experienced more significant sequelae than helmeted males and suffered more serious symptoms than males without helmets. Among all unhelmeted athletes, females were more than twice as likely as males to experience cognitive impairment following concussion (57 compared with 28%, respectively). Based on these data, it seems clear that females experience more objective and subjective adverse effects of concussion even after adjusting for the wearing of protective head gear.

Another possible explanation for the sex-based differences in our study may be related to the style of play or level of aggressiveness inherent in different sports. Sports played by males are typically assumed to be more aggressive, which is part of the reason helmets are often required even though the same sport played by females does not (for example, lacrosse), although this theory may not be accurate. Future investigators must examine the sex differences in the on-field behavior as well as the mechanisms of sports-related concussion.

From a physiological perspective, sex differences in hormonal systems, cerebral organization, and musculature may partially explain our findings. The literature provides contrary findings regarding the potential neural protection afforded by female gonadal hormones in animals. Estrogen may be either a protective or a detrimental factor depending on the study reviewed, whereas progesterone seems to function broadly to reduce post-TBI neural impairment.³⁴ The varying results may be a reflection of study design, including whether animals were exposed to a fluid-percussion injury, a focal-impact injury, or an impact-acceleration injury. In addition, authors of a recent study, which demonstrated that estrogen provided a neuroprotective effect in female mice, did not manipulate levels of estrogen but simply examined differences in recovery based on sex.²⁷ In contrast, other researchers who found that estrogen exacerbated brain injuries in female rats and provided protective effects in male rats actually treated the rats with supplemental estrogen 4 hours prior to inducing head injury.¹⁶ These discrepant findings may be partially due to the differential impact of exogenous compared with endogenous estrogen in TBI. Future research in humans should be aimed at examining fluctuations in hormonal levels to determine whether there are cyclical periods of greater vulnerability or greater neuroprotection in concussed female athletes that might affect neurocognitive outcome, the recovery curve, and the duration of follow up.

The fact that sex may differentially determine TBI incidence, severity, and symptom resolution should not be surprising. There are considerable sex-based differences in neural anatomy and physiology, cerebrovascular organization, and cellular response to concussive stimuli. For example, cortical neuronal densities are greater in males, whereas neuropil numbers are greater in females.¹² Blood flow rates are greater in females than in males,¹⁹ and females exhibit a greater basal rate of glucose metabolism.¹ The latter two functional differences may well exist in support of the increased ionic flux across the greater membrane area suggested by the higher neuropil count. To the extent

TABLE 3
*Frequency of cognitive impairment on postconcussion follow up in 131 athletes**

Group	No. of Patients (%)	
	w/o Cognitive Impairment	w/ Cognitive Impairment
unhelmeted males	13 (72.2)	5 (27.8)
helmeted males	50 (65.8)	26 (34.2)
unhelmeted females	16 (43.2)	21 (56.8)

* $\chi^2 = 6.52$, $p = 0.038$.

that brains in females may have greater metabolic demands, a more intense and prolonged symptom response to mild TBI may reflect an exacerbated, or at least a more broadly distributed, metabolic cascade as described by Giza and Hovda.²² Specifically, the typical decrease in cerebral blood flow along with the increased glycemic demands caused by TBI may interact with the already increased demands and lead to greater impairment in females than in males.

Although there was no significant sex-based difference in performance on baseline neurocognitive testing, one of the limitations of this study is that no inference can be made about baseline sex differences in intellectual ability or cognitive reserve based on the test administered. It is possible that any differences might have affected the observed sex effect in concussion outcome. Furthermore, we only examined postconcussive sex differences among athletes for whom we had baseline neurocognitive data, perhaps resulting in selection bias. Our study design of obtaining baseline data in large numbers of athletes in high-risk sports, however, limits the impact of this confound. In addition, the length of time between concussion and follow-up neurocognitive evaluation was not standardized among all the data collection sites. Interestingly, although female athletes tended not to be followed up as quickly—thus allowing additional time for recovery—they still demonstrated poorer outcomes.

Data in this study provide important information for the clinical management of concussion. Note that although females experienced more severe postconcussion symptoms, males were followed up significantly sooner (by approximately 24 hours), perhaps indicating that injuries in females may not be taken as seriously. Alternatively, this finding may reflect less aggressive follow-up testing based on the perceived severity of initial symptoms and conservative management of the recovery process (that is, not performing cognitive challenges while the patient remains symptomatic). Results of previous studies have revealed a tendency for females to report more symptoms following head injury.^{6,35} Those in the medical profession often interpret such reports as an indication that women complain more despite having fewer objective symptoms. Based on objective test findings, we assert that females do in fact experience more severe postconcussion symptoms than males and that poorer outcomes are not simply due to culturally based sex differences in reporting symptoms. Such findings may be critical in countering the documented reduced levels of post-TBI services provided to women.⁵

Because more severe objective declines in reaction time and processing speed mirrored more severe subjective symptoms, data in this study serve to caution against dismissing symptom reports following TBI. Although post-

concussion syndrome symptoms may represent nonneurological factors,²⁴ clearly such is not universally true. Although male athletes were more likely to experience LOC at the time of concussion, which may have been interpreted as reflecting a more severe injury, women demonstrated worse cognitive dysfunction on follow up. This finding provides additional evidence for the growing literature indicating that LOC is not a good predictor of outcome.^{10,18,28} Again, our results call into question the return-to-play criteria (such as those of the AAN) that rely heavily on LOC in grading concussion. Although current investigators still use LOC as the only measure of severity,³³ many authors have pointed out the shortcomings in this approach.^{8,40,41} Although, intuitively, the approach of using baseline neurocognitive testing to detect changes following concussion appears more sensitive than traditional grading scales, we did not perform a direct comparison of these two approaches in the present study. It remains a critical area for future research.

Conclusions

Female athletes had significantly more severe declines on SRTs and CRTs relative to preseason baseline levels and they reported more postconcussion symptoms compared with males. Furthermore, females were cognitively impaired approximately 1.7 times more often than males following concussion. Females experienced more objective and subjective adverse effects of concussion even after adjusting for the use of helmets by some groups of male athletes (for example, those playing football). Given the potential for sex differences and other as yet unidentified variables that affect concussion severity and recovery, the importance of individualized concussion management cannot be overstated. Data collected on the preseason baseline administration of computerized or paper-and-pencil neuropsychological measures that are validated for detecting concussion for comparison with individual postconcussion data represent the gold standards for identifying the degree of cognitive decline and recovery. Medical care and return-to-play decisions should be based on a comparison between pre- and postinjury neurocognitive data and the recovery curve of each individual athlete rather than relying on one-size-fits-all return-to-play criteria.

Disclosure

Drs. David Erlanger and Tanya Kaushik are employed by Head-Minder, Inc., which is the publisher of the CRI. Dr. Erlanger also holds a significant number of shares in the company.

References

1. Andreason PJ, Zametkin AJ, Guo AC, Baldwin P, Cohen RM: Gender-related differences in regional cerebral glucose metabolism in normal volunteers. *Psychiatry Res* 51:175–183, 1994
2. Barth JT, Alves WM, Ryan TV, et al: Mild head injury in sports: Neuropsychological sequelae and recovery of function, in Levin HS, Eisenberg HM, Benton AL (eds): *Mild Head Injury*. New York: Oxford Press, 1989, pp 257–275
3. Barth JT, Freeman JR, Broshek DK: Mild head injury, in Ramachandran VS (ed): *Encyclopedia of the Human Brain*. San Diego: Academic Press, 2002, Vol 3, pp 81–92
4. Bazarian JJ, Wong T, Harris M, Leahey N, Mookerjee S, Dombrov M: Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. *Brain Inj* 13:173–189, 1999
5. Bounds TA, Schopp L, Johnstone B, Unger C, Goldman H: Gender differences in a sample of vocational rehabilitation clients with TBI. *NeuroRehabilitation* 18:189–196, 2003
6. Brooks J: Gender issues in brain injury, in Lovell MR, Echemendia R, Barth JT, et al. (eds): *Traumatic Brain Injury in Sports*. Lisse, The Netherlands: Swets & Zeitlinger, 2004, pp 443–466
7. Cantu RC: Guidelines for return to contact sports after a cerebral concussion. *Phys Sportsmed* 14:75–83, 1986
8. Cantu RC: Posttraumatic retrograde and anterograde amnesia: pathophysiology and implications in grading and safe return to play. *J Athl Train* 36:244–248, 2001
9. Centers for Disease Control and Prevention: **Traumatic Brain Injury (TBI): Risks & Groups at Risk**. (<http://www.cdc.gov/node.do/id/0900f3ec8000dbdc/aspectId/C60308>) [Accessed 23 February 2005]
10. Collins MW, Iverson GL, Lovell MR, McKeag DB, Norwig J, Maroon J: On-field predictors of neuropsychological and symptom deficit following sports-related concussion. *Clin J Sport Med* 13:222–229, 2003
11. Covassin T, Swanik CB, Sachs ML: Sex differences and the incidence of concussions among collegiate athletes. *J Athl Train* 38:238–244, 2003
12. de Courten-Myers GM: The human cerebral cortex: gender differences in structure and function. *J Neuropathol Exp Neurol* 58:217–226, 1999
13. Donders J, Hoffman NM: Gender differences in learning and memory after pediatric traumatic brain injury. *Neuropsychology* 16:491–499, 2002
14. Donders J, Woodward HR: Gender as a moderator of memory after traumatic brain injury in children. *J Head Trauma Rehabil* 18:106–115, 2003
15. Echemendia RJ, Julian LJ: Mild traumatic brain injury in sports: neuropsychology's contribution to a developing field. *Neuropsychol Rev* 11:69–88, 2001
16. Emerson CS, Headrick JP, Vink R: Estrogen improves biochemical and neurologic outcome following traumatic brain injury in male rats, but not in females. *Brain Res* 608:95–100, 1993
17. Erlanger D, Feldman D, Kutner K, Kaushik T, Kroger H, Festa J, et al: Development and validation of a web-based neuropsychological test protocol for sports-related return-to-play decision-making. *Arch Clin Neuropsychol* 18:293–316, 2003
18. Erlanger D, Kaushik T, Cantu R, Barth JT, Broshek DK, Freeman JR, et al: Symptom-based assessment of the severity of a concussion. *J Neurosurg* 98:477–484, 2003
19. Esposito G, Van Horn JD, Weinberger DR, Berman KF: Gender differences in cerebral blood flow as a function of cognitive state with PET. *J Nucl Med* 37:559–564, 1996
20. Farace E, Alves WM: Do women fare worse: a metaanalysis of gender differences in traumatic brain injury outcome. *J Neurosurg* 93:539–545, 2000
21. Fenton G, McClelland R, Montgomery A, MacFlynn G, Rutherford W: The postconcussional syndrome: social antecedents and psychological sequelae. *Br J Psychiatry* 162:493–497, 1993
22. Giza CC, Hovda DA: The pathophysiology of traumatic brain injury, in Lovell MR, Barth JT, Collins MW (eds): *Traumatic Brain Injury in Sports*. Lisse, The Netherlands: Swets & Zeitlinger, 2004, pp 45–70
23. Grosswasser Z, Cohen M, Karen O: Female TBI patients recover better than males. *Brain Inj* 12:805–808, 1998
24. Gunstad J, Suhr JA: Cognitive factors in Postconcussion Syndrome symptom report. *Arch Clin Neuropsychol* 19:391–405, 2004
25. Kozniowska E, Roberts TPL, Vexler ZS, Oseka M, Kucharczyk J, Arieff AI: Hormonal dependence of the effects of metabolic encephalopathy on cerebral perfusion and oxygen utilization in the rat. *Circ Res* 76:551–558, 1995

26. Kraus JF, Peek-Asa C, McArthur D: The independent effect of gender on outcomes following traumatic brain injury: a preliminary investigation. **Neurosurg Focus** 8(1):E5, 2000
27. Kupina NC, Detloff MR, Bobrowski WF, Snyder BJ, Hall ED: Cytoskeletal protein degradation and neurodegeneration evolves differently in males and females following experimental head injury. **Exp Neurol** 180:55–73, 2003
28. Lovell MR, Iverson GL, Collins MW, McKeag D, Maroon JC: Does loss of consciousness predict neuropsychological decrements after concussion? **Clin J Sport Med** 9:193–198, 1999
29. McCrea M, Kelly J, Randolph C: **The Standardized Assessment of Concussion (SAC): Manual for Administration and Scoring**. Alexandria, VA: The Brain Injury Association, 1997
30. Mueller FO: Catastrophic head injuries in high school and collegiate sports. **J Athl Train** 36:312–315, 2001
31. Report of the Quality Standards Subcommittee: practice parameter: the management of concussion in sports (summary statement). **Neurology** 48:581–585, 1997
32. Rimel RW, Giordani B, Barth JT, Boll TJ, Jane JA: Disability caused by minor head injury. **Neurosurgery** 9:221–228, 1981
33. Rohling ML, Meyers JE, Millis SR: Neuropsychological impairment following traumatic brain injury: a dose-response analysis. **Clin Neuropsychol** 17:289–302, 2003
34. Roof RL, Hall ED: Gender differences in acute CNS trauma and stroke: neuroprotective effects of estrogen and progesterone. **J Neurotrauma** 17:367–388, 2000
35. Rutherford WH, Merrett JD, McDonald JR: Symptoms at one year following concussion from minor head injuries. **Injury** 10: 225–230, 1979
36. Ryan JP, Atkinson TM, Dunham KT: Sports-related and gender differences on neuropsychological measures of frontal lobe functioning. **Clin J Sport Med** 14:18–24, 2004
37. United States Department of Education: **Title IX: 25 years of progress**. (<http://www.ed.gov/pubs/TitleIX/index.html#toc>) [Accessed 24 February 2005]
38. Vriezen ER, Pigott S: Gender differences in executive function following pediatric brain injury, in **International Neuropsychological Society Conference, Baltimore, MD, 2004, 32nd Annual Meeting Program & Abstracts**. Columbus, OH: International Neuropsychological Society, p 50 (Abstract)
39. Waber DP, Mullenix PJ: Acute lymphoblastic leukemia, in Yeates KO, Ris MD, Taylor HG (eds): **Pediatric Neuropsychology: Research, Theory, and Practice**. New York: Guilford Press, 2000, pp 300–319
40. Webbe FM: Cerebral concussion: definition, physiology, and severity, in Echemendia RJ (ed): **Sports Neuropsychology: A Clinical Primer**. New York: Guilford Press (In press)
41. Webbe FM, Barth JT: Short-term and long-term outcome of athletic closed head injuries. **Clin Sports Med** 22:577–592, 2003
42. Women's Sports Foundation: **Title IX: Overview of Current Developments**. (<http://www.womenssportsfoundation.org/cgi-bin/iowa/about/media/press.html?record=68>). [Accessed 24 February 2005]

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